CLAIMS

1. A method of selecting a microorganism, composition, vaccine or vaccine component, for use in treatment or prevention of disease caused by Gram negative bacteria, comprising determining whether said microorganism, composition, vaccine or vaccine component is substantially free of Opa that binds *CEACAM1*.

2. A method according to Claim 1 wherein said microorganism, composition, vaccine or vaccine component is selected to be substantially free of Opa that binds *CEACAM1* or is modified so as to be substantially free of Opa that binds *CEACAM1*.

3. A method according to Claim 1 or Claim 2, wherein said Gram negative bacteria is selected from *Neisseria*, *Moraxella*, *Kingella*, *Acinetobacter*, *Brucella*, *Bordetella*, *Porphyromonas*, *Actinobacillus*, *Borelia*, *Serratia*, *Campylobacter*, *Helicobacter*, *Haemophilus*, *Escherichia*, *Legionella*, *Salmonella*, *Pseudomonas* and *Yersinia*.

4. A method according to Claim 3, wherein said microorganism is a Neisseria.

5. A method of selecting a microorganism, composition, vaccine or vaccine component, for use in treatment or prevention of meningococcal disease or gonococcal disease, comprising determining whether said microorganism, composition, vaccine or vaccine component is substantially free of protein that suppresses activation or proliferation of a CD4+ T cell.

6. A method according to Claim 5 wherein said microorganism, composition, vaccine or vaccine component is selected to be substantially free of Opa that binds *CEACAM1* or is modified so as to be substantially free of Opa that binds *CEACAM1*.

7. A method according to Claim 5, wherein said microorganism, composition, vaccine or vaccine component is substantially free of Opa that binds *CEACAM1*.

8. A method according to Claim 5, wherein said microorganism is a Neisseria.

9. A method according to Claim 4 or 8, wherein said Neisseria is selected to be substantially free of Opa that binds *CEACAM1* or is modified so as to be substantially free of Opa that binds *CEACAM1*.

10. A method according to Claim 9, wherein said Neisseria is modified by mutation.

11. A microorganism, composition, vaccine or vaccine component obtained according to any of Claims 1 to 10.

12. A population of Gram negative bacteria, being 1,000 or more in number, substantially free of bacteria expressing Opa that binds *CEACAM1*.

13. A composition, comprising neisseria outer membrane vesicles, wherein the vesicles are substantially free of Opa.

14. A composition according to Claim 13, wherein the Opa content of the vesicles is reduced by at least a factor of 10 compared with the Opa content of OMVs obtained from normal neisseria.

15. A composition according to Claim 13 or 14 wherein Opa represents 1% or less by weight of the total protein content of OMVs.

16. A composition according to any of Claims 13-15, further comprising a pharmaceutically acceptable carrier.

17. A composition according to any of Claims 13-16, for vaccination.

18. A composition, comprising neisseria outer membrane vesicles, wherein the vesicles comprise an Opa protein that does not bind to *CEACAM1*.

19. A composition according to Claim 18, substantially free of Opa that binds *CEACAM1*.

20. A composition, comprising neisseria outer membrane vesicles, wherein the vesicles comprise a protein which:-

is antigenic,

elicits production of antibodies which bind to Opa, and

does not bind to *CEACAM1*.

21. A composition according to Claim 20 wherein the protein is a mutant or fragment or variant or derivative or mimic of Opa.

22. A composition, comprising neisseria outer membrane vesicles, wherein the vesicles comprise an antagonist which inhibits binding of Opa to *CEACAM1*.

23. A method of preparing a composition for use as or in manufacture of a vaccine, the method comprising:-
(a) obtaining a Gram negative bacterium;
(b) determining whether the bacterium expresses an Opa protein that binds to *CEACAM1*;
(c) if the bacterium expresses the Opa protein, discarding the bacterium and repeating steps (a) to (c);
(d) retaining the bacterium if it does not express the Opa protein; and
(e) preparing a composition comprising the retained bacterium of step (d).

24. A method according to Claim 23, wherein the bacterium is a *Neisseria*.

25. A method according to Claim 23 or 24, comprising retaining a bacterium which expresses a mutant or variant or fragment or derivative of Opa, wherein the mutant or variant or fragment or derivative does not bind to *CEACAM1*.

26. A method according to any of Claims 23 to 25, comprising preparing an outer membrane vesicle from the retained bacterium.

27. A method of obtaining a mutant or variant or fragment or derivative or mimic of Opa, the method comprising:-
(a) obtaining a Gram negative bacterium;
(b) carrying out mutagenesis on the bacterium;
(c) determining whether the bacterium expresses a mutant or fragment or variant

or derivative or mimic of an Opa protein that does not bind to *CEACAM1*;
(d) isolating the mutant or variant or fragment or derivative or mimic.

28. A method according to Claim 27, wherein the bacterium is a *Neisseria*.

29. A method according to Claim 27 or 28, further comprising:-
(e) raising an antibody to the mutant or fragment or variant or derivative or mimic; and
(f) determining whether the antibody also binds to an Opa protein that binds to *CEACAM1*.

30. A mutant or variant or fragment or derivative of Opa, wherein the mutant or variant or fragment or derivative does not bind to *CEACAM1*.

31. A method of treatment or prevention of disease, comprising administering a microorganism, composition, vaccine or vaccine component of Claim 11, or a population of Gram negative bacteria of Claim 12 or composition according to any of Claims 13 to 22.

32. A vaccine comprising a microorganism, composition, vaccine or vaccine component of Claim 11, or a population of Gram negative bacteria of Claim 12 or composition according to any of Claims 13 to 22.

33. A method of manufacture or testing of a vaccine, the method comprising:-
(a) obtaining a sample of a vaccine or of a component of a proposed vaccine against a Gram negative bacteria; and
(b) determining whether the sample contains an Opa protein that binds to *CEACAM1*.

34. A method according to Claim 33, further comprising:-
(c) determining the weight % of the Opa protein, if present, by weight % of total protein content in the vaccine or in the sample.

35. A method according to Claim 33 or 34, comprising:-
(d) rejecting the vaccine or the component if the sample contains the Opa protein, or if the weight% of the Opa protein is above a predetermined level.

36. Use of *Neisseria* outer membrane vesicles which (i) are substantially free of Opa, (ii) comprise an Opa protein that does not bind to *CEACAM1*, (iii) comprise a mutant or fragment or derivative of Opa that does not bind to *CEACAM1*, or (iv) comprise an antagonist which inhibits binding of Opa to *CEACAM1*, in manufacture of a medicament for treatment or prevention of meningococcal disease with improved stimulation of immune memory or reduced inhibition of T cell function.

37. A method of obtaining a mutagenised Opa gene, comprising (a) cloning an Opa gene, (b) inserting the cloned gene into an expression vector, and (c) mutagenising the cloned gene.

38. A method according to Claim 37, further comprising expressing a protein from the gene obtained from (c), isolating the protein and testing the protein for (i) binding to *CEACAM1*, and / or (ii) generating antibodies that bind to native Opa.

39. A composition comprising a protein obtained according to a method of Claim 37 or 38.

40. A gene encoding a protein, wherein (a) the protein does not bind to *CEACAM1*, and (b) antibodies to the protein bind native Opa.

41. A gene obtained according to Claim 37 or a protein obtained according to Claim 38.

42. A vector containing a gene according to Claim 40 or 41

43. A cell comprising a gene according to Claim 40 or 41.